#### Curriculum Vitae

## John Ernest Sims

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Date of Birth: March 11, 1947

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Education

1965-1969 Harvard College, Cambridge, Massachusetts

Degree: B.A. cum laude, June 1969

1969-1970 University of Pennsylvania School of Medicine

Philadelphia, Pennsylvania

1970-1979 Harvard University, Department of Biochemistry

and Molecular Biology, Cambridge, Massachusetts

Degree: Ph.D., June 1979

1979-1983 Post-doctoral fellow, laboratories of T. Rabbitts

and C. Milstein, MRC Laboratory of Molecular Biology, Cambridge, England

**Employment** 

1983-1984 Staff, Medical Research Council Laboratory of Molecular Biology, Cambridge,

England

1984-1988 Staff Scientist, Molecular Biology Department,

Immunex Corporation, Seattle, Washington

1989-1990 Senior Staff Scientist,

Immunex Corporation, Seattle, Washington

1990-1992 Head, Division of Gene Discovery

Department of Molecular Biology

Immunex Corporation, Seattle, Washington

1993-2000 Director

Department of Molecular Genetics

Immunex Corporation, Seattle, Washington

2000-2002 Senior Director

Department of Molecular Genetics

Immunex Corporation, Seattle, Washington

2002 Vice President

Department of Molecular Biology

Immunex Corporation, Seattle, Washington

2002- Present Distinguished Fellow

Molecular Immunology Amgen, Seattle, Washington

### **Activities**

Editorial Board, Journal of Interferon & Cytokine Research, 1991-Present

Ad hoc reviewer for journals:

Analytical Biochemistry, Brain Research, Circulation, Clinical & Experimental Metastasis, Cytokine, Endocrinology, European Cytokine Network, European Journal of Cell Biology, European Journal of Immunity, Human Molecular Genetics, Immunity, International Journal of Immunopharmacology, International Journal on Genes & Genomes, Journal of Clinical Investigation, Journal of Immunology, Journal of Molecular Biology, Laboratory Investigation, Life Sciences, Molecular Immunology, PNAS, Virology

Ad hoc reviewer for grants:

Welcome Trust, Canadian MRC, NIH (Allergy, Immunological Sciences Study Sections) Arthritis Research Council, United Kingdom

### **Patents**

U.S. Patent 5,296,592 (2001-F) Process for Purifying Interleukin-1 Receptors

U.S. Patent 5,319,071 (2001-E) Soluble Interleukin-1 Receptors

U.S. Patent 5,350,683 (2003-D)
DNA Encoding Type II Interleukin-1 Receptors

U.S. Patent 4,968,607 (2001-A) Interleukin-1 Receptors

U.S. Patent 5,081,228 (2001-B) Interleukin-1 Receptors

U.S. Patent 5,180,812 (2002)
Soluble Human Interleukin-1 Receptors, Compositions and Method of Use

### Patents (Continued)

U.S. Patent 5,422,248

DNA Sequences Encoding Granulocyte-Colony Stimulating Factor Receptors

U.S. Patent 5,464,937

Type II Interleukin-1 Receptors

U.S. Patent 5,488,032

Method of Using Soluble Human Interleukin-1 Receptors to Suppress Inflammation

U.S. Patent Re 3540

Soluble Human Interleukin-1 Receptors, Compositions and Method of Use

U.S. Patent 5,492,888

Method of Using Soluble Human Interleukin-1 Receptors to Suppress Immune Responses

U.S. Patent 5,576,191

Cytokine that Binds ST2

U.S. Patent 5,589,456

Granulocyte-Colony Stimulating Factor Receptors

U.S. Patent 5,767,064

Soluble Type II Interleukin-1 Receptors and Methods

U.S. Patent 5,776,731

DNA Encoding Type-I Interleukin-1 Receptor-Like Protein Designated 2F1

U.S. Patent 6,080,557

IL-1/TNF-α-Activated Kinase (ITAK, and Methods of Making and Using the Same)

U.S. Patent 6,090,918

Receptor Protein Designated 2F1

U.S. Patent 6,451,760 B1

Treatment of Inflammation Using A 2F1 Polypeptide Or An Antibody Thereto

U.S. Patent 6,541,232 B1

Polypeptides Having Kinase Activity

U.S. Patent 6,511,665 B1

Antibodies to Interleukin-1 Receptors

U.S. Patent 6,555,520 B2

Human TSLP DNA and Polypeptides

U.S. Patent 6,521,740 B1

Type II Interleukin-1 Receptors

U.S. Patent 6,589,764 B1

IL-18 Receptor Fusion Proteins

# **Published Patent Cooperation Treaty (PCT) Applications**

PCT Serial No. PCT/US88/03926 Publication No. WO 89/04838 Interleukin-1 Receptors

PCT Serial No. PCT/US90/05434
Publication No. WO 91/05046
Granulocyte-Colony Stimulating Factor Receptors

PCT Serial No. PCT/US91/03498 Publication No. WO 91/18982 Type II Interleukin-1 Receptors

PCT Serial No. PCT/US97/00690 Publication No. WO 97/25347 IL-1 Receptor Interacting Protein

PCT Serial No. PCT/US97/01697 Publication No. WO 97/31010 Receptor Protein Designated 2F1

PCT Serial No. PCT/US97/08516
Publication No. WO 97/47750
IL-1/TNF-alpha-Activated Kinase (ITAK, and Methods of Making and Using the Same)

PCT Serial No. PCT/US98/27368 Publication No. WO 99/32626 SIGIRR DNA and Polypeptides

PCT Serial No. PCT/US98/27625 Publication No. WO 99/32629 TIGIRR DNA and Polypeptides

PCT Serial No. PCT/US99/00514 Publication No. WO 99/35268 IL-1 Delta DNA and Polypeptides

PCT Serial No. PCT/US99/01420 Publication No. WO 99/37773 ACPL DNA and Polypeptides

PCT Serial No. PCT/US99/01419 Publication No. WO 99/37772 IL-18 Receptors

PCT Serial No. PCT/US99/23533 Publication No. WO 00/20595 Interleukin-1 Homolog

#### **Research Publications**

- 1. Sims, J. and Dressler, D. 1978. Site-specific initiation of a DNA fragment: Nucleotide sequence of the bacteriophage G4 negative strand initiation site. Proc. Natl. Acad. Sci. USA 75, 3094-3098.
- 2. Sims, J., Koths, K. and Dressler, D. 1978. Single-stranded phage replication: Positive-and negative-strand DNA synthesis. Cold Spring Harbor Symposium 43, 349-365.
- 3. Sims, J., Capon, D. and Dressler, D. 1979. dnaG (Primase)-dependent origins of DNA replication: Nucleotide sequences of the negative strand initiation sites of bacteriophages St-1, φK and α3. J. Biol. Chem. 254, 12615-12628.
- Sims, J. and Benz, E. 1980. Initiation of DNA replication by the Escherichia coli dnaG protein: Evidence that tertiary structure is involved. Proc. Natl. Acad. Sci. USA 77, 900-904.
- 5. Benz, E., Sims, J., Dressler, D. and Hurwitz, J. 1980. Tertiary structure is involved in the initiation of DNA synthesis by the dnaG protein. In: ICN-UCLA Symposium on Molecular and Cellular Biology. Mechanistic Studies of DNA Replication and Genetic Recombination. Alberts, B. (ed.) Academic Press, New York, pp. 279-291.
- 6. Sims, J., Rabbitts, T.H., Estess, P., Slaughter, C., Tucker, P.W. and Capra, J.D. 1982. Somatic mutation in genes for variable portion of the immunoglobulin heavy chain. Science 216, 309-311.
- 7. Sims, J., Tunnacliffe, A., Smith, W.J. and Rabbitts, T.H. 1984. Complexity of human T-cell antigen receptor β-chain constant- and variable-region genes. Nature 312, 541-545.
- 8. Rabbitts, T.H., Lefranc, M.P., Stinson, M.A., Sims, J.E., Schroder, J., Steinmetz, M., Spurr, N.L., Solomon, E. and Goodfellow, P.N. 1985. The chromosomal location of T-cell receptor genes and a T cell rearranging gene: Possible correlation with specific translocations in human T cell leukemia. EMBO J. 4, 1461-1465.
- 9. Tunnacliffe, A., Sims, J.E. and Rabbitts, T.H. 1986. T3δ pre-mRNA is transcribed from a non-TATA promoter and is alternatively spliced in human T cells. EMBO J. 5, 1245-1252.
- Sims, J.E., March, C.J., Cosman, D., Widmer, M.B., MacDonald, H.R., McMahan, C.J., Grubin, C.E., Wignall, J., Jackson, J.L., Call, S.M., Friend, D., Alpert, A., Gillis, S., Urdal, D.L. and Dower, S.K. 1988. cDNA expression cloning of the receptor for interleukin-1, a member of the immunoglobulin superfamily. Science 241, 585-589.
- 11. Morrissey, P.J., Goodwin, R.G., Cosman, D., Sims, J.E., Lupton, S. Acres, B., Reed, S.G. and Namen, A.E. 1989. Recombinant IL-7, pre B cell growth factor, has costimulatory activity on purified mature T cells. J. Exp. Med. 169, 707-716.
- 12. Curtis, B.M., Gallis, B., Overell, R., McMahan, C.J., de Roos, P., Eisenman, J., Dower, S.K. and Sims, J.E. 1989. The T cell IL-1 receptor cDNA expressed in CHO cells regulates functional responses to IL-1. Proc. Natl. Acad. Sci. USA 86, 3045-3049.

- 13. Dower, S.K., Wignall, J., Schooley, K., McMahan, C.J., Jackson, J., Prickett, K.S., Lupton, S., Cosman, D. and Sims, J.E. 1989. Retention of ligand binding activity by the extracellular domain of the IL-1 receptor. J. Immunol. 142, 4314-4320.
- Mosley, B., Beckmann, M.P., March, C.J., Idzerda, R.L., Gimpel, S.D., VandenBos, T., Friend, D., Alpert, A., Anderson, D., Jackson, J., Wignall, J.M., Smith, C., Gallis, B., Sims, J.E., Urdal, D., Widmer, M.B., Cosman, D. and Park, L.S. 1989. The murine interleukin-4 receptor: Molecular cloning and characterization of secreted and membrane bound forms. Cell 59, 335-348.
- 15. Bomsztyk, K., Sims, J.E., Stanton, T.H., Slack, J., McMahan, C.J., Valentine, M.A. and Dower, S.K. 1989. Evidence for different interleukin 1 receptors in murine B- and T-cell lines. Proc. Natl. Acad. Sci. USA 86, 8034-8038.
- Gallis, B., Prickett, K.S., Jackson, J., Slack, J., Schooley, K., Sims, J.E. and Dower, S.K.
   1989. Interleukin-1 induces rapid phosphorylation of the IL-1 receptor. J. Immunol. 143, 3235-3240.
- 17. Sims, J.E., Acres, R.B., Grubin, C.E., McMahan, C.J., Wignall, J.M., March, C.J. and Dower, S.K. 1989. Cloning of the interleukin-1 receptor from human T cells. Proc. Natl. Acad. Sci. USA 86, 8946-8950.
- 18. Slack, J., Sims, J.E., Pitt, A.M. and Dower, S.K. 1989. Application of the multiscreen system to cytokine radioreceptor assays. BioTechniques 7, 1132-1138.
- 19. Fanslow, W.C., Sims, J.E., Sassenfeld, H., Morrissey, P.J., Gillis, S., Dower, S.K. and Widmer, M.B. 1990. Regulation of alloreactivity in vivo by a soluble form of the interleukin-1 receptor. Science 248, 739-742.
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- 21. Munoz, E., Zubiaga, A.M., Sims, J.E. and Huber, B.T. 1990. IL-1 signal transduction pathways. I. Two functional IL-1 receptors are expressed in T cells. J. Immunol. 146, 136-143.
- 22. Spriggs, M., Lioubin, P., Slack, J. Cosman, D., Sims, J. and Bauer, J. 1990. Induction of an interleukin-1 receptor (IL-1R) on monocytic cells. Evidence that the receptor is not encoded by a T cell-type IL-1R mRNA. J. Biol. Chem. 265, 22499-22505.
- 23. Larsen, A., Davis, T., Curtis, B.M., Gimpel, S., Sims, J.E., Cosman, D., Park, L., Sorensen, E., March C.J. and Smith, C.A. 1990. Expression cloning of a human granulocyte colony-stimulating factor receptor: A structural mosaic of hematopoietin receptor, immunoglobulin, and fibronectin domains. J. Exp. Med. 172, 1559-1570.

- Ostrowski, J., Sims, J., Sibley, C., Valentine, M., Dower, S., Meier, K., and Bomsztyk, K. 1991. A serine/threonine kinase activity is closely associated with a 65-kDa phosphoprotein specifically recognized by the κB enhancer. J. Biol. Chem. 266, 12722-12733.
- 25. Bird, T.A., Woodward, A., Jackson, J.L., Dower, S.K. and Sims, J.E. 1991. Phorbol ester induces phosphorylation of the 80 kilodalton murine interleukin 1 receptor at a single threonine residue. Biochem. Biophys. Res. Comm. 177, 61-67.
- McMahan, C.J., Slack, J.L., Mosley, B., Cosman, D., Lupton, S.D., Brunton, L.L., Grubin, C.E., Wignall, J.M., Jenkins, N.A., Brannan, C.I., Copeland, N.G., Huebner, K., Croce, C.M., Cannizzarro, L.A., Benjamin, D., Dower, S.K., Spriggs, M.K. and Sims, J.E. 1991. A novel IL-1 receptor, cloned from B cells by mammalian expression is expressed in many cell types. EMBO J. 10, 2821-2832
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- 29. Spriggs, M.K., Hruby, E.E., Maliszewski, C.R., Pickup, D.J., Sims, J.E., Buller, M.L., and VanSlyke, J. 1992. Vaccinia and cowpox viruses enclde a novel secreted interleukin-1-binding protein. Cell 71:145-152.
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- 31. Slack, J., McMahan, C.J., Waugh, S., Schooley, K., Spriggs, M.K., Sims, J.E. and Dower, S.K. 1993. Independent binding of interleukin-1α and interleukin-1β to type I and type II IL-1 receptors. J. Biol. Chem. 268, 2513-2524.
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- 33. McKean, D.J., Podzorski, R.P., Bell, M.P., Nilson, A.E., Huntoon, C.J., Slack, J., Dower, S.K. and Sims, J. 1993. Murine T helper cell-2 lymphocytes express type I and type II IL-1 receptors, but only the type I receptor mediates costimulatory activity. J. Immunol. 151:3500.

- 34. Sims, J.E., Gayle, M.A., Slack, J.L., Alderson, M.R., Bird, T.A., Giri, J.G., Colotta, F., Re, F., Mantovani, A., Shanebeck, K., Grabstein, K.H. and Dower, S.K. 1993. Interleukin-1 signalling occurs exclusively via the type I receptor. Proc. Natl. Acad. Sci. USA 90, 6155-6159.
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- 36. Gayle, M.A., Sims, J.E., Dower, S.K. and Slack, J.L. 1994. Monoclonal antibody 1994:01 (also known As Alva 42) reported to recognize Type II IL-1 receptor is specific for HLA-DR alpha and beta chains. Cytokine. 4:1, 83-86.
- 37. Arend, W. P., Malyak, M., Smith, M. F. Jr., Whisenand, T. D., Slack, J. L., Sims, J. E., Giri, J. G., Dower, S. K. 1994. Binding of IL-1α, IL-1β, and IL-1 receptor antagonist by soluble IL-1 receptors and levels of soluble IL-1 receptors in synovial fluids. J. Immunol. 153:10, 4766-4774.
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- 39. Groves, R.W., Giri, J., Sims, J., Dower, S.K., and Kupper, T.S. 1995. Inducible expression of type 2 IL-1 receptors by cultured human keratinocytes. J. Immunol. 154:8, 4065-4072.
- 40. Sims, J., Painter, S., Gow, I. 1995. Genomic organization of the Type I and Type II IL-2 receptors. Cytokine. 7:6, 483-490.
- 41. Parnet, P., Garka, K.E., Bonnert, T.P., Dower, S.K., and Sims, J.E. 1996. IL-1 Rrp is a novel receptor-like molecule similar to the Type I IL-1 receptor and its homologues T1/ST2 and IL-1R AcP. J. Biol. Chem. 271(8), 3967-3970.
- 42. Mitcham, J.L., Parnet, P., Gerhart, M.J., Garka, K.E., Taguchi, T., Testa, J.R., Gayle, M.A., Slack, J.L., Dower, S.K., and Sims, J.E. 1996. T1/ST2 signaling establishes it as a member of an expanding IL-1 receptor family. J. Biol. Chem 271, 5777-5783.
- 43. Gayle, M.A., Slack, J.L., Bonnert, T.P., Renshaw, B.R., Sonoda, G., Taguchi, T., Testa, J.R., Dower, S.K., and Sims, J.E. 1996. Cloning of a putative ligand for the T1/ST2 receptor. J. Biol. Chem. 271, 5784-5789.
- 44. Taguchi, T., Mitcham, J.L., Dower, S.K., Sims, J.E., and Testa, J.R. 1996. Chromosomal localization of TIL, a gene encoding a protein related to the drosophila transmembrane receptor toll, to human chromosome 4p14. Genomics 32, 486-488.

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- 46. Colotta, F., Saccani, S., Giri, J.G., Sims, J.E., Introna, M., and Mantovani, A. 1996. Regulated expression and release of the Interleukin 1 (IL-1) decoy receptor in human mononuclear phagocytes. J. Immunol. 156, 2534-2541.
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   Modulation of osteoblast-activating factor activity of multiple myeloma bone marrow cells by different Interleukin-1 inhibitors. Exp. Hem. 24:8, 868.
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- 54. Thomassen, E., Renshaw, B.R., Sims, J.E., 1999. Identification and characterization of SIGIRR, a molecule representing a novel subtype of the IL-1R superfamily. CYTOKINE, Vol. 11, No. 6(June), 1999; pp 389-399.
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- 67. Smith, D.E., Ketchem, R.R., Moore, H., Anderson, Z., Renshaw, B.R., Sims, J.E. A Single Amino Acid Difference between Human and Monkey IL-1β Dictates Effective Binding to Soluble Type II IL-1 Receptor. J Biol Chem 2002 December 277(49):47619-47625.
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#### Reviews

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